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Via Facsimile
571-273-8300

Examiner Tigabu Kassa
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Re: Controlled-Release Pharmaceutical Formulation
Sandoz Reference No. PAT033571-US-PCT
U.S. Application Serial No. 10/583,440
Filed June 16, 2006
Applicant: Polonca KUHAR
LNG File No. 64654.US/ C-6710.0.Slovenia

Dear Examiner Kassa:

In reference to the Advisory Action issued April 13, 2010, in the above case, please see the attached copies of published data sheets for the EUDRAGIT L30D-55 and EUDRAGIT NE 30D products discussed by the Examiner in the Advisory Action.

The Examiner correctly notes from the specification that Applicant teaches use of EUDRAGIT NE 30D as a suitable polymer material for satisfying the requirements of the claims relative to the composition of the pellet cores. As the Examiner knows, the claims require, among other things, that the pellet cores release the "low dose" tamsulosin in a controlled manner "independent of pH," and that the cores contain a water-insoluble polymer that is also permeable to the ingress/egress of water. This polymer appears to be the crux of the matter insofar as the Advisory Action is concerned.

The Examiner also correctly notes Applicants' specification of EUDRAGIT

NE30D as a polymer in the pellet cores that provides the desired pH-independent water-insoluble permeability for controlled release of the tamsulosin from the pellet cores.

The Examiner further correctly notes Platteeuw's teaching to use the polymer EUDRAGIT L30D-55 in the pellet cores of Patteeuw's tamsulosin composition. In this regard, the Examiner argues that these EUDRAGIT materials taught by Applicants and by Platteeuw in the tamsulosin pellet core are the "same." The Examiner contends that the EUDRAGIT NE 30D polymer material specified by Applicants in the pellet cores of their claimed composition and the EUDRAGIT L30D-55 polymer material specified by Platteeuw in its pellet core composition are only different in "syntax," and that there are no differences in "composition content."

Applicants respectfully disagree with Examiner's contentions, and they urge the Examiner to reconsider his position on the alleged identicality of EUDRAGIT NE30D and EUDRAGIT L30D-55. The identicality/non-identicality of these polymeric materials is a matter of central importance to this case. Applicants should be afforded the opportunity to respond to the Examiner's assertion now, so it can be determined whether a clear issue has been developed in regard to this critically important matter.

At no point prior to the Advisory Action did the Examiner contend that his rejection was founded on an alleged identicality between the polymeric material EUDRAGIT NE30D taught by Applicants for use as the "water insoluble permeable polymer" in the pellet cores for release of the tamsulosin "independent of pH," and the polymeric material EUDRAGIT L30 D55 taught by Platteeuw for inclusion in the pellet core of their composition. In other words, the Examiner now alleges that the polymeric material EUDRAGIT L30 D-55 mentioned by Platteeuw is a permeable "water insoluble polymer" that would, upon inclusion in a pellet core, provide a controlled release of tamsulosin "independent of pH" according to the requirements of Applicants' claims. The Examiner's basis for this is his contention that EUDRAGIT NE 30D specified by Applicants and EUDRAGIT L30 D-55 specified by Platteeuw are "the same."

The attached materials show that the EUDRAGIT L30 D-55 product referred to by Platteeuw for inclusion in their pellet core is in fact "Ph-dependent," and that it dissolves in

water at a pH above 5.5 (a neutral pH is about 7.0). In fact, EUDRAGIT L30 D-55 is "pH-sensitive" (dissolving at pH 5.5 or higher). On the other hand, the EUDRAGIT NE30D product specified by Applicants as the polymer material for the core in the claimed compositions is "pH independent" and "insoluble."

Accordingly, the basis for the Examiner's conclusions in the Advisory Action of April 13, 2010, about the alleged identicality of these polymer materials are, with all due respect, entirely wrong. These materials are virtual opposites, and are very far from what anyone of ordinary skill could reasonably say are the "same." The mere fact that both materials belong to the family of EUDRAGIT products does not mean they are the same, or that they have the same properties. It is evident from the manufacturer's chart attached hereto that the products in question are profoundly different, and that no person of ordinary skill would reasonably select EUDRAGIT L30 D55 for inclusion in a pharmaceutical tamsulosin composition in the form of a pellet having the characteristics/ properties specified in Applicants' claims.

Accordingly, the Examiner's rationale for maintaining the rejection of Applicants' claims as set forth in the Advisory Action is manifestly erroneous.

MPEP §706.07 cautions that "[b]efore final rejection is in order a clear issue should be developed between the examiner and applicant." This admonition applies with great force in the present case, where an assertion of central importance to the viability of the rejection is raised for the first time in an Advisory Action in an effort to support continued rejection of Applicants' claims, and has been shown beyond question to be flat wrong, and therefore a fundamentally improper basis for maintaining the current rejection, much less making the rejection final. It is plain that no clear issue is or ever was developed with regard to the nature of the EUDRAGIT materials as they relate to requirements in Applicants' claims that very plainly are not satisfied by materials used in the pellet core compositions taught by the cited art.

Given the above and the fact that maintenance of this rejection hinges on a clearly erroneous belief about the identicality of materials referenced in the prior art vis-a-vis materials used to in the current claims, Applicants urge the Examiner to withdraw the current rejection and allow the claims in order to avoid useless additional prosecution/appeal proceedings and

associated waste of time and expense for both Applicants and the USPTO.

Please be kind enough to withdraw the rejection, or, at the very least, allow the undersigned the opportunity to discuss this matter with the Examiner and his Supervisor before any further action is taken.

If you have any questions, please call. Otherwise, we look forward to hearing from you at your earliest convenience.

Best regards.

Yours very truly,

LUEDEKA, NEELY & GRAHAM, P.C.

By: Mark S. Graham

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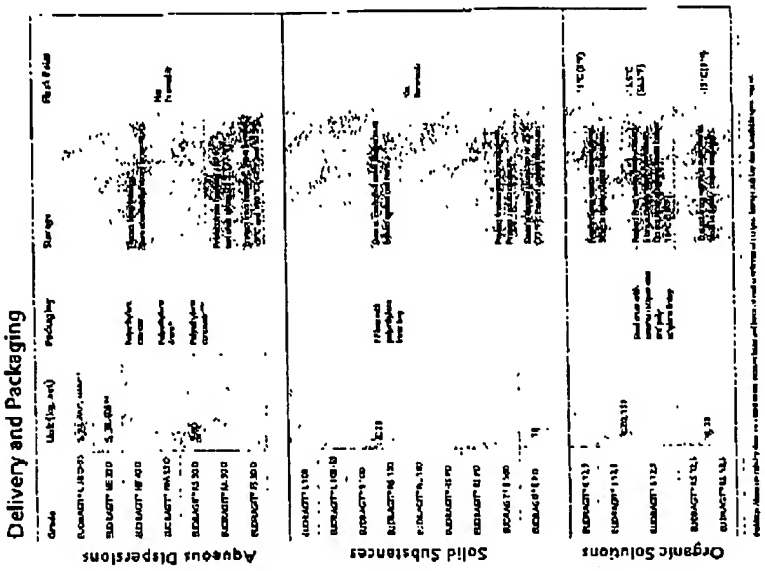
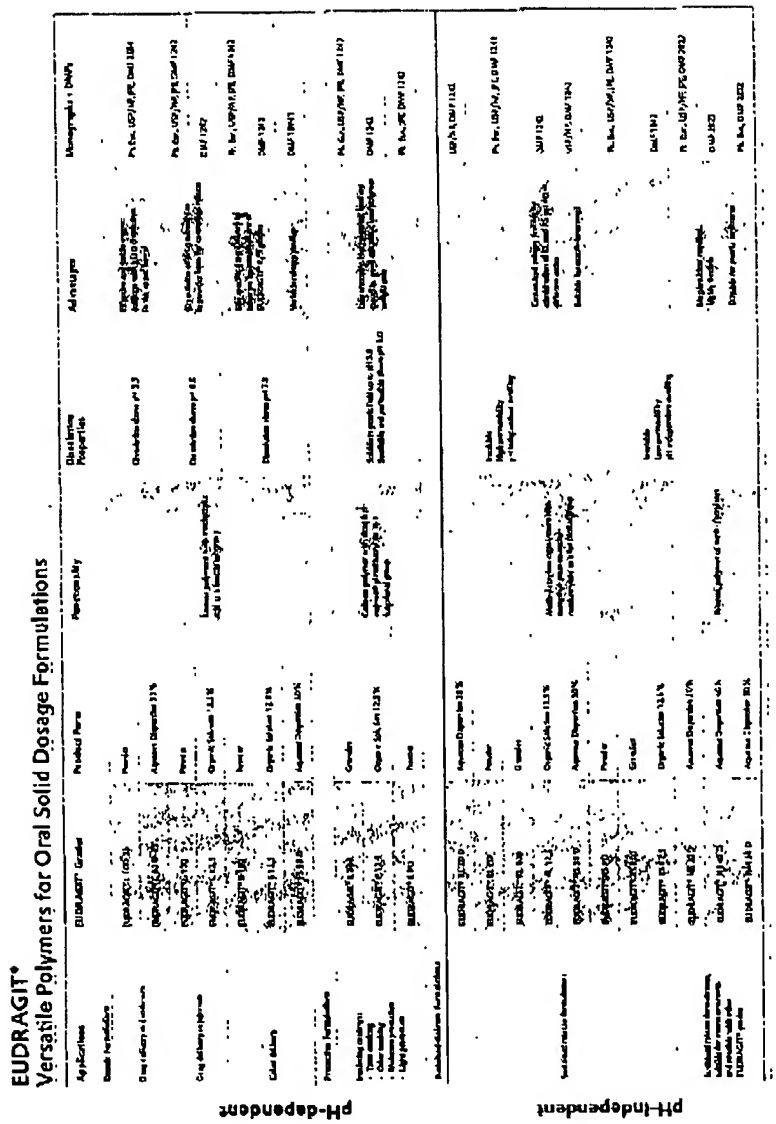
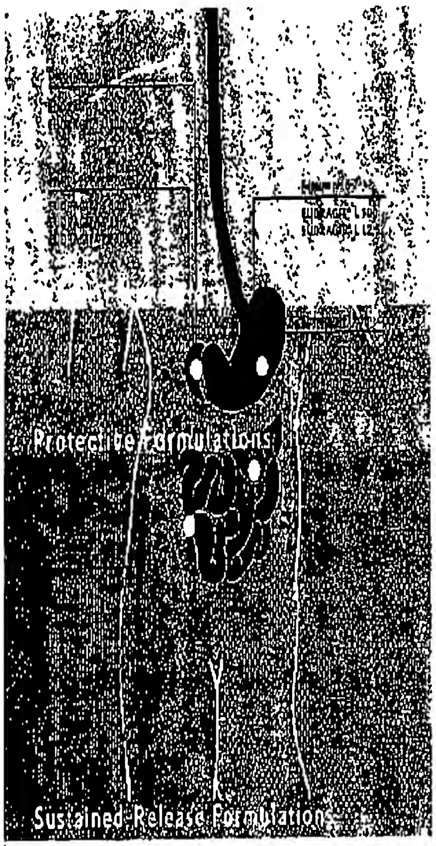

Delivery and Packaging
Aqueous Dispersions
Solid Substances
Organic Solutions


EUDRAGIT®
Versatile Polymers for Oral Solid Dosage Formulations
pH-dependent
pH-independent

EUDRAGIT®

Versatile Polymers for Oral Solid Dosage Formulations



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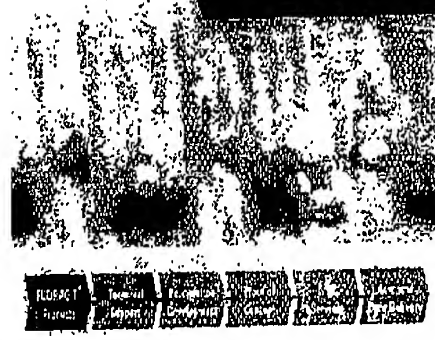
EUDRAGIT®

at a glance



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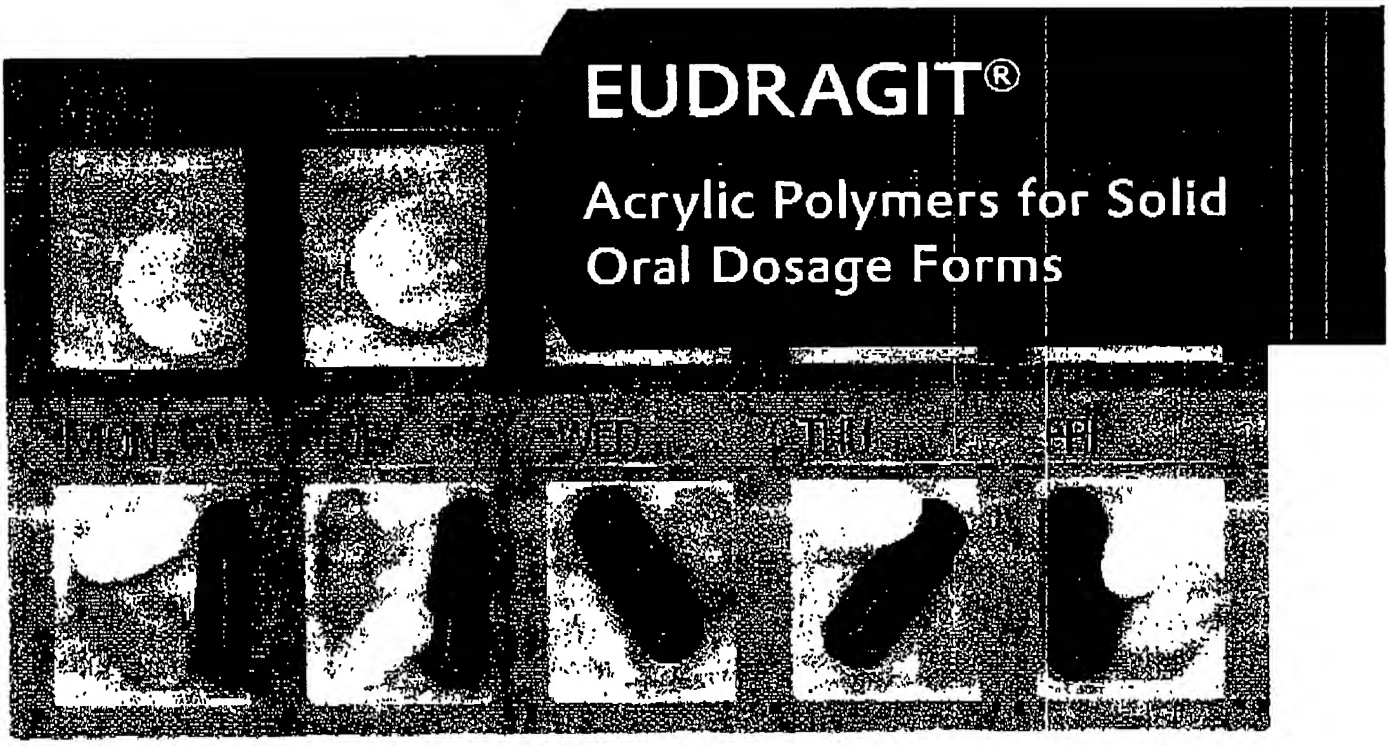
EVONIK INDUSTRIES

EUDRAGIT®

Acrylic Polymers for Solid Oral Dosage Forms



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EUDRAGIT® Polymers – Pharmaceutical Properties

The basis of our offerings are our Poly(meth)acrylates for pharmaceutical applications, which are known worldwide in the industry under the trade name EUDRAGIT®. These polymers allow the active in your solid dosage form to perform during the passage of the human body. The flexibility to combine the different polymers enables you to achieve the desired drug release profile by releasing the drug at the right place and at the right time and, if necessary, over a desired period of time. Other important functions are protection from external influences (moisture) or taste/odor masking to increase patient compliance. The range of our product portfolio provides full flexibility for your targeted drug release profiles by offering best performance for enteric, protective or sustained-release properties.

EUDRAGIT® polymers are copolymers derived from esters of acrylic and methacrylic acid, whose physicochemical properties are determined by functional groups (R). EUDRAGIT® polymers are available in a wide range of different physical forms (aqueous dispersion, organic solution granules and powders).

A distinction is made between 1. Poly(meth)acrylates; soluble in digestive fluids by salt formation EUDRAGIT® L, S, FS and E polymers with alkaline groups enable pH-dependent release of the active ingredient. Applications from simple taste masking through gastric resistance to controlled drug release in all sections of the intestine

2. Poly(meth)acrylates; insoluble but permeable in digestive fluids EUDRAGIT® RL and RS polymers with alkaline and EUDRAGIT® NE polymers with neutral groups enable controlled time release of the active ingredient by pH-independent swelling. Applications: delayed and sustained drug release

Enteric Formulations

EUDRAGIT® offers valuable advantages for your enteric coatings:

- pH-dependent drug release
- Protection objectives sensitive to gastric fluid
- Protection of gastric mucosa from aggressive actives
- Increase in drug effectiveness
- Good storage stability
- GI and colon targeting

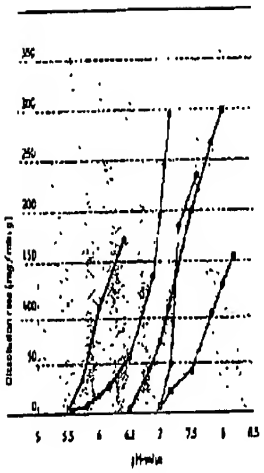
Gastroresistance and GI Targeting

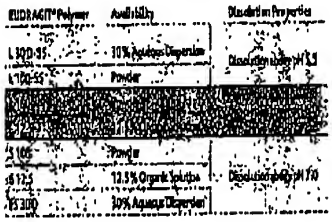
If you need to protect your active from the gastric fluid and would like to improve drug effectiveness – EUDRAGIT® L and S polymers are your preferred choice of coating polymers. They enable targeting specific areas of the intestine. Pharma Polymers offers a broad product portfolio of anionic EUDRAGIT® grades which dissolve at rising pH values. In addition, the different grades can be combined with each other, making it possible to adjust the dissolution pH, and thus to achieve the required GI targeting for the drug.

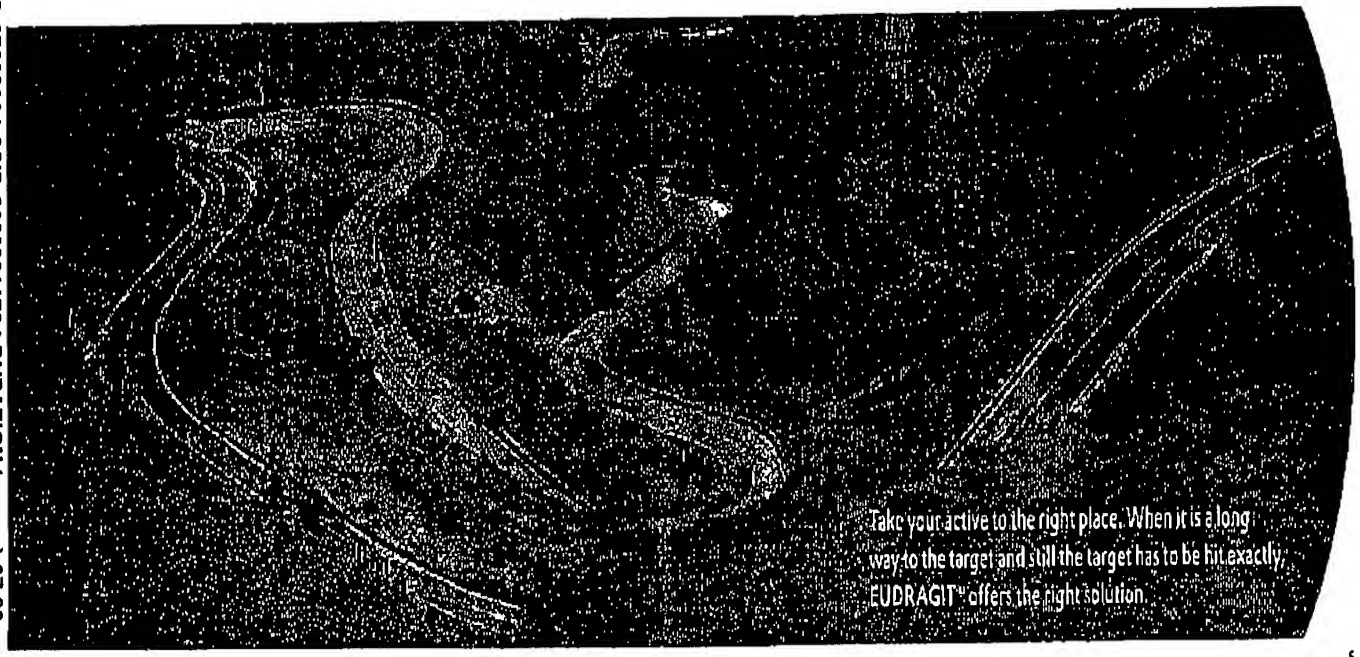
Targeted drug release in the colon is required for local treatment of intestinal disorders such as Crohn's disease, ulcerative colitis or intestinal cancer. It is also required for drugs that are poorly soluble in the upper gastrointestinal tract. Moreover, the gastroresistance of the coating ensures that the oral dosage form is patient compliant.

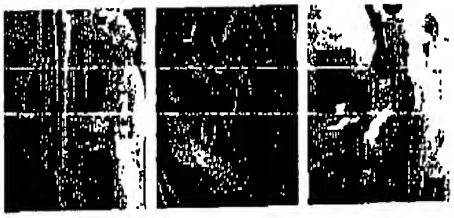
The preferred coating is EUDRAGIT® FS 30 D, which combines release in the colon with the following technical advantages:

- aqueous processing
- highly flexible coatings
- suitable for multiparticulate tablet preparation









Our protective polymers are suitable for aqueous or organic coatings and can be applied in a melt extrusion process. During the melt extrusion process the excipient EUDRAGIT® E polymer interacts with the anionic active which provides excellent taste masking properties.

Moisture Protection and Odor/Taste Masking

Do you need to protect your active from moisture or light and would like to increase patient compliance?

EUDRAGIT® E polymers help you to seal sensitive actives and increase patient compliance by masking tastes and odors. Even thin layers of EUDRAGIT® provide the desired effect, making it an extremely economical application. Pharma Polymers offer various cationic EUDRAGIT® E grades for protective coatings.

EUDRAGIT® Polymer	Availability	Dissolution Properties
E100	Granule	Soluble in gastric fluid up to pH 5.0
E12,5	12.5 % Organic Solution	Swells in and permeable above pH 5.0
E PO	Powder	

Take advantage of protective EUDRAGIT® coatings!

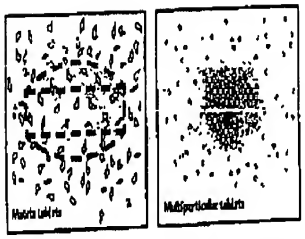
- pH-dependent drug release
- Protection of sensitive actives
- Taste and odor masking
- Moisture protection
- Economical application
- Improved passage of the dosage form
- Smooth and glossy surfaces, good color coating

EUDRAGIT® offers a broad protection for sensitive contents and improves patient compliance.

Sustained Release Formulations

Time-Controlled Drug Release

Whether you need your drug to release over a specific period of time or would like to benefit from the advantages of multi-particulate or matrix formulations – EUDRAGIT® can help you achieve your desired release profile. Drug delivery can be controlled throughout the entire gastrointestinal tract to increase therapeutic effect and patient compliance. Different polymer combinations of EUDRAGIT® RL and RS grades allow custom-tailored release profiles to achieve the desired drug delivery performance. EUDRAGIT® NE and NM grades are neutral ester dispersions which do not require addition of plasticizer.

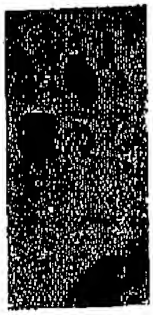


There are two formulation options:

EUDRAGIT® serves as a matrix within which the active ingredients embedded. The matrix structure is obtained by direct compression, granulation, or melt extrusion. EUDRAGIT® Fate 100 is particularly suitable for granulation processes in the manufacture of matrix tablets.

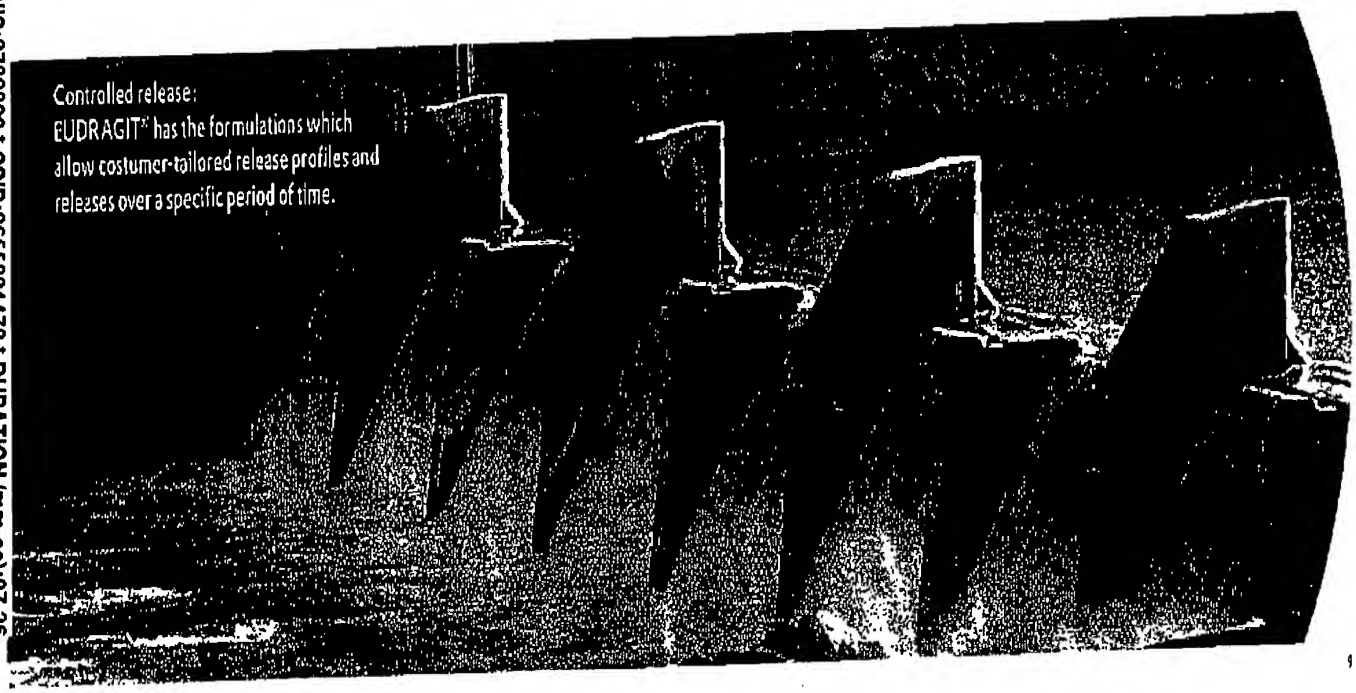
EUDRAGIT® is employed as a coating material, usually for the coating of pellets or particles that are filled into capsules or compressed into tablets. These pellets or particles act as diffusion cells in the digestive tract and release a constant drug quantity per unit of time (multi-unit dosage forms).

EUDRAGIT® Polymer	Availability	Dissolution Properties
RL 100	Granules	Insoluble
RL PO	Powder	High permeability
RL 30D	30% Aqueous Dispersion	pH-independent swelling
RL 12.5	12.5% Organic Solution	
RS 100	Granules	Insoluble
RS PO	Powder	Low permeability
RS 30D	30% Aqueous Dispersion	Insoluble, low permeability, pH-independent swelling
NE30D	30% Aqueous Dispersion	pH-independent swelling
NE40D	40% Aqueous Dispersion	Insoluble, low permeability, pH-independent swelling
NM30D	30% Aqueous Dispersion	Non-plasticized, modified RS 30 D equivalent



Benefit from EUDRAGIT® coatings with sustained release:

- Time-controlled release of active ingredients
- Therapeutically customized release profiles
- Higher patient compliance due to reduced number of doses to be taken
- Cost-effective processing



Value Chain

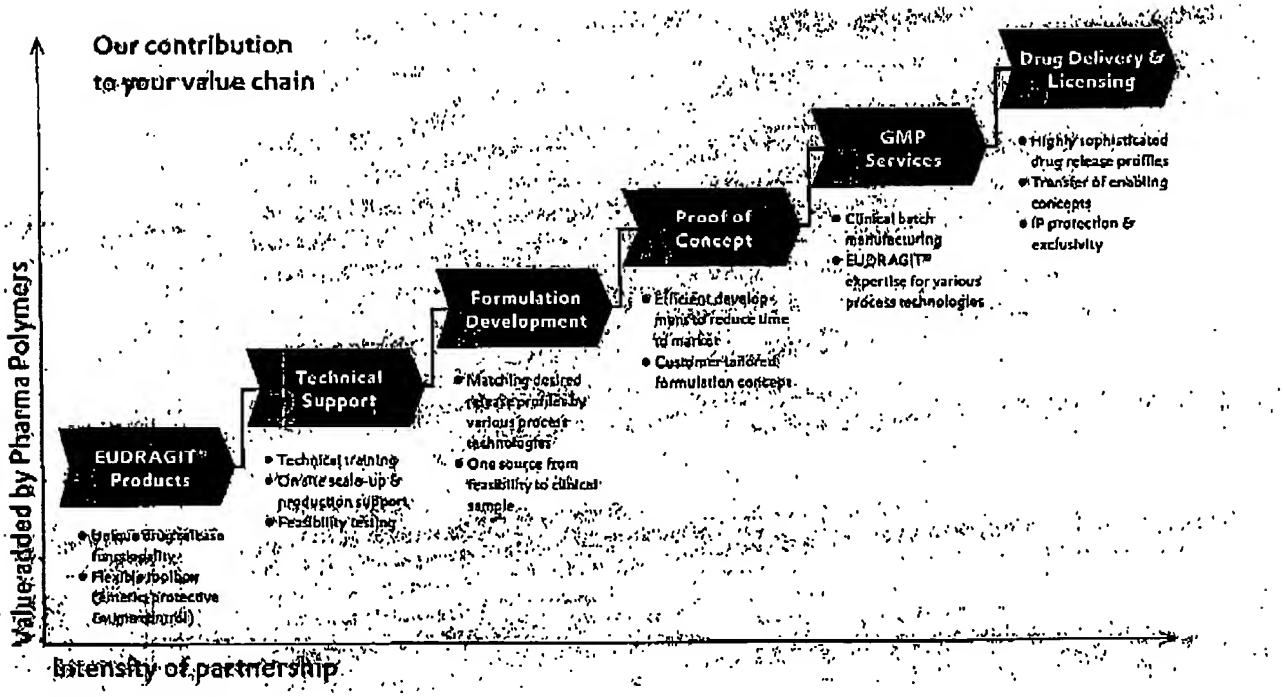
Market Strength by means of Strategic Partnership

Pharma Polymers, a business line of Evonik Industries, offers the complete line of EUDRAGIT® products and related services along the value chain of our customers. For over 50 years we have proven our reliability as a quality partner to the pharmaceutical industry. Our state of the art services cover various stages of the development processes, including

- advanced technical support
- formulation development
- proof of concept
- GMP services.

Our customers see us as a strategic partner for their developments of solid oral dosage forms with a targeted drug release profile. By using our value adding business model our customers get:

- increased efficiency in their R&D and manufacturing processes
- new drug delivery technologies
- reduction of the time to market for their developments
- professional management of their product's life cycle



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